Acids of Many Uses From Corn

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Most of the commercial sugar acids come from dextrose, the sugar derived from corn. They are cheap and mild and, chemically, maids-of-all-work. Their uses range from the simple process of cleaning milk cans and bottles to the complex production of vitamins.

Veterinarians and farmers know best the calcium salt of gluconic acid, which they use for the treatment of milk fever in cows and which doctors sometimes recommend for bee stings.

The housewife is most familiar with cream of tartar, an ingredient of the baking powder she uses for her pies and cakes. Citric acid, the acid that gives the tang to citrus fruits, she also uses for flavoring lemon pies. Its magnesium salt—citrate of magnesia—has often been prescribed as a laxative for her family. No doubt she is also acquainted with ascorbic acid, the sugar acid that is made in chemical factories and is the same as the vitamin C in oranges and lemons.

Chemists have known about the sugar acids for a long time, but new uses for them are being discovered constantly. For instance, doctors recently learned that glucuronic acid, first isolated from the body in 1875, may relieve the pains of rheumatism and sciatica.

The versatile nature of the sugar acids has aroused increasing interest in them as raw materials for the production of such things as plastics, detergents, and medicines. More attention is being given, consequently, to the development of practical methods for obtaining them from dextrose.

Processes for the fermentation of dextrose to citric, gluconic, 2-ketogluconic, 5-ketogluconic, α-ketoglutaric, and itaconic, and similar acids have been developed in the laboratories of the Department of Agriculture. Some, particularly those for citric and gluconic acids, have achieved commercial importance. The large-scale production of itaconic acid appears promising. Lactic acid, a widely used food acid, is being produced in large volumes by the corn-products industries by fermentation of cornstarch hydrolyzates.

The acids I have mentioned have also been made by nonfermentative methods, but of the purely chemical processes only those for obtaining gluconic and itaconic acids merit consideration from a practical standpoint. Some years ago workers at the National Bureau of Standards devised a procedure for the electrolytic oxidation of corn sugar to gluconic acid. It appears to be competitive with the fermentation method. The electrolysis is carried out between carbon electrodes in the presence of bromides and calcium carbonate buffer, and the gluconic acid is neutralized as it is formed to give calcium gluconate.

Itaconic acid was originally produced in pilot-plant quantities from citric acid. The dehydration of citric acid with mineral acids yields aconitic acid, which is readily decarboxylated to itaconic acid. More recently, however, chemists at the Southern Regional Research Laboratory have demonstrated that the calcium magnesium aconitate present in sugarcane molasses can be recovered in commercial amounts without significantly altering the processing of the molasses for sugar production. A practical method was also devised for converting the crude alkaline-earth aconitate to itaconic acid of high purity. It has been estimated that at least 4 million pounds of aconitic acid a year are potentially available as a byproduct of the sugarcane grown and milled in Louisiana and Florida alone. In 1950 there was a demand for at least a million pounds of aconitic acid for conversion to esters for plasticizers. The remaining 3 million pounds of potential production would yield about 2 million pounds of itaconic acid for use in the manufacture of plastics, detergents and such.

The sugar acids—levulinic, tartaric, ascorbic, isoascorbic, arabonic, saccharic, and glucuronic acids—cannot be produced at all, or only inefficiently, by the direct fermentation of dextrose. When not derived from natural sources, they are generally made by chemical conversion of dextrose.

Levulinic acid has been manufactured on a commercial scale by heating starch hydrolyzates with mineral acids. The low cost, stability, and chemical activity of this interesting keto acid have encouraged its development from both a practical and a theoretical standpoint. Some of the compounds that have been synthesized from levulinic acid have been found to possess local anesthetic and analgesic action. Others have bactericidal and detergent properties.

Since the beginning of the century, practical methods for the synthesis of tartaric acid have been sought. The search has been stimulated by the increased use of the acid and its salts and by our dependence upon foreign sources of argols, the crude potassium bitartrate that crystallizes in wine barrels, from which most commercial tartaric acid is made. In the Second World War, the shortage of argols brought the price of tartaric acid up from about 40 cents to more than 70 cents a pound. To alleviate this situation, processes were devised to recover the residual tartrates in domestic grape pomace and in brandy-still slop. These significant developments were achieved by chemists in commercial wineries and at the Western Regional Research Laboratory. At the Atlas Powder Company, pilot-plant experiments had also been carried out for the production of tartaric acid by the nitric acid oxidation of dextrose. Still another method of synthesis is the catalytic oxidation of 5-ketogluconic acid by oxygen. The raw material for this process, calcium 5-ketogluconate, can readily be produced by a biological process developed in the Department of Agriculture.

Because of the low cost of tartaric acid, the synthetic processes are not now being used. However, the tartrates in grape wastes are being successfully recovered on a large scale. It is estimated that 10 million pounds of tartaric acid is potentially recoverable from grape residues. Because of the threat of the synthetic processes, the price of tartaric acid may never again rise to the exorbitant levels reached in 1941 to 1946.

Various ascorbic acids are known. They can be prepared from corn sugar as the starting material. The most important one, vitamin C, has the chemical name *l*-xyloascorbic acid. It is used mainly in the treatment of scurvy and other diseases due to vitamin C deficiency. It is thought that subnormal amounts of ascorbic acid in the body lead to ready infection with such diseases as rheumatic fever, tuberculosis, and diphtheria.

Of secondary importance is the compound *d*-araboascorbic acid, which is usually called isoascorbic acid. The ascorbic acids have the same general formula, except that the hydroxyl group on the fifth carbon atom of each has an opposite spatial position. Both of these substances have similar antioxidant properties, but isoascorbic acid has only one-twentieth the antiscorbutic activity of vitamin C. Vitamin C is found in nature in citrus fruits, cabbage, paprika, pine needles, and walnuts. It is generally produced commercially by the Reichstein process (or a modification of it), whereby dextrose is catalytically hydrogenated to *d*-sorbitol, which may then be fermented to *l*-sorbose by a method developed by Department of Agriculture scientists. The sorbose is reacted with acetone in the presence of sulfuric acid to form diacetone sorbose. Alkaline solutions of the diacetone sorbose are oxidized with potassium permanganate or sodium hypochlorite to diacetone 2-keto-*l*-gulonic acid, which, when hydrolyzed, yields 2-keto-*l*-gulonic acid. This acid may be esterified with methanol and then transformed to vitamin C by the action of sodium methylate, or it may be converted directly to vitamin C by heating with hydrochloric acid. By an analogous procedure, the methyl ester of 2-keto-*d*-gluconic acid is rearranged to produce isoascorbic acid.

THE CHIEF VALUE of *d*-arabonic acid lies in its use as an intermediate in the chemical synthesis of riboflavin—vitamin B_2. The riboflavin molecule contains a carbohydrate residue, which is derived from *d*-ribose. The 5-carbon sugar, *d*-ribose, is generally obtained from the nucleic acids found in yeast cells or from dextrose and arabinose, via arabonic acid. Arabonic acid is usually produced by the oxidation of corn sugar in alkaline solution with oxygen or air. In 1946, however, a new method of preparation was developed at the Northern Regional Research Laboratory. In it, calcium 2-ketogluconate is electrolytically oxidized to calcium arabonate in 85 percent yield, in a manner similar to that used for the production of gluconic acid. Apparently in this reaction decarboxylation of the 2-ketogluconic acid first occurs. The resulting product is immediately oxidized to arabonic acid, which is neutralized by the excess calcium carbonate present. Pure calcium arabonate pentahydrate crystals are obtained by evaporation of the filtered oxidation liquor.

The arabonic acid obtained from the calcium salt is rearranged to *d*-ribonic acid by heating it in pyridine solution, a process called epimerization. By devious and costly methods, *d*-ribonic acid may be converted to *d*-ribose for use in the riboflavin synthesis. Processes have recently been developed, however, whereby ribose can be prepared directly by the electrolytic reduction of ribonolactone. The ribose is isolated as an aniline-ribose-sodium sulfate complex from which the ribose can readily be obtained in crystalline form. It is believed that this development will reduce the cost of making ribose to such an extent as to revive interest in the production of crystalline riboflavin by chemical means.

SACCHARIC ACID is more correctly named *d*-glucosaccharic acid or *d*-glucaric acid, because it is the dibasic sugar acid derived from *d*-glucose by oxidation of the terminal groups. Although saccharic acid has been prepared by the nitric acid oxidation of corn sugar and starch for more than a century, no practical method for its large-scale production had been devised until 1948. Chemists at the Northern Laboratory have now developed a feasible process for making saccharic acid in yields nearly twice as great as those previously obtained. In this process, corn sugar is gradually added to concentrated nitric acid so as to maintain the temperature of the reaction at about 60° C. After several hours the oxidation mixture is neutralized with potassium hydroxide and then adjusted to the desired acidity with nitric acid to precipitate practically pure potassium acid saccharate in 40 to 45 percent yield.

The white crystalline product is filtered, washed free of contaminating salts with water, and dried. It may be converted to calcium saccharate by reaction with a mixture of calcium chloride and lime. Saccharic acid may be obtained by the addition of sufficient sulfuric acid to remove the calcium ions as insoluble calcium sulfate.

Investigation of the practical applications of the acid and its salts is now in progress.

Glucuronic acid is of great physiological importance. A detoxifying agent in the animal body, it reacts with such poisons as phenols and amines to form innocuous glucuronides, which are eliminated in the urine. It is also a significant constituent of fibrous tissue and of heparin, the blood anticoagulant that is present in many of these body tissues. The specific polysaccharide of type III pneumococcus, which possesses immunological reactivity, has also been shown to contain glucuronic acid in its structure. In 1947 an apparent correlation between glucuronic acid deficiency and rheumatic diseases was discovered and the successful treatment of a number of such cases with salts of glucuronic acid has been reported. The use of glucuronic acid as a detoxicant in sulfa therapy has also been indicated.

Although numerous attempts to prepare this important acid have been made in the past, no practical chemical syntheses were available until 1950, when the Northern Regional Research Laboratory and Corn Products Refining Co. independently announced processes for its production. In the Northern Laboratory process, corn sugar is reacted with acetone and the product catalytically oxidized to acetone glucuronic acid with air. Simple hydrolysis of acetone glucuronic acid produces glucuronic acid which is isolated in good yield as crystalline glucuronolactone. Translation of these new processes to large-scale operation will expedite both therapeutic and industrial research on this sugar acid.

Calcium salts of gluconic, lactic, arabonic, and levulinic acids are being used in the treatment of calcium deficiencies in the human and animal body. Because in water solution they are practically neutral, they are less irritating to the skin upon injection than the calcium salts of the inorganic acids. They are also more palatable when taken by mouth. With the exception of calcium levulinate, the calcium salts of the sugar acids are not soluble enough in water for their efficient utilization in the treatment of lactating cows for hypocalcemia, or milk fever. It is often necessary to inject as much as 50 to 75 grams of calcium gluconate into the jugular vein of a cow in a single dose. Such a treatment would require as much as 1 to 2 quarts of a saturated calcium gluconate solution.

Various methods have been successful in increasing the solubility of calcium gluconate. The introduction of boric acid results in the formation of soluble calcium borogluconate, which has been found to be an effective source of calcium in veterinary medicine. Also in use are stable supersaturated solutions of calcium gluconate of at least 10 percent concentration, made by the addition of small amounts of stabilizing substances, as calcium saccharate, calcium salts of sulfonic acids, and strontium salts. The solubility of calcium sodium lactate in water has also been enhanced by the addition of calcium gluconate.

Since the discovery in 1906 that antimony compounds are effective therapeutic agents for the treatment of the protozoan diseases, African sleeping sickness and kala-azar, the death rate from those diseases has declined enormously. One of the original substances tried and one that still is in use for the control of the diseases is the potassium antimonyl salt of tartaric acid. Another sugar acid antimonial, sodium antimonyl gluconate, has been reported helpful in the treatment of kala-azar.

Tartaric acid in combination with bismuth, as bismuth sodium tartrate or bismuth potassium tartrate, has been used intramuscularly to obtain the systemic effect of bismuth in the treatment of syphilis. Bismuth potassium saccharate has also been used.

Water solutions of iron, copper, and manganese salts of sugar acids are used to obtain the effects of the respective

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metal ions. Sodium lactate has been indicated for the prevention and treatment of acidosis, and aqueous solutions of magnesium citrate have been used for many years as a saline laxative. More recently, citric acid and sodium citrate have become important for the preservation of whole blood. It appears also that sodium citrate may have value in the treatment of lead poisoning. Lactic acid has been used effectively as an aerial bactericide. Ascorbic acid has been reported to be useful in the healing of wounds. Recently, calcium gluconate solutions have been found of value in the treatment of bee stings. Phenyl mercuric tartrate, gluconate, saccharate, and lactate have been prepared for bactericidal purposes. The use of such compounds as ephedrine gluconate, procaine gluconate, gluconophenetid, and ergotamine tartrate has been indicated for the treatment of various ailments.

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VARNISHES were used in Egypt on mummy cases of the New Empire. Many are insoluble, but their method of preparation is not known with certainty. The earliest mention of the use of a drying oil in a process connected with painting is given by Aetius, about the sixth century. He stated that nut oils dry and form a protective varnish. From that time on, the use of drying oils and varnishes seems to be well established and formulas for transparent varnishes composed of linseed oil and natural resins dating from the eighth or ninth century after Christ are known.

Theophilus Presbyter, an obscure craftsman, who lived at the end of the eleventh century, used linseed oil with some kind of resin, probably amber, copal, or sandarac, to prepare oil colors. He worked out many formulas for paints, varnishes, and dyes. However, the discovery of the effect of driers in linseed-oil paints, which is accredited to the brothers Van Eyck, was not made until the first half of the fifteenth century.

The extensibility of oil on the surface of water appears to have been known to Greek sailors, who used oil to subdue waves during a storm. The phenomenon of surface tension of extension of oil on the surface of water was investigated by the great Hindu mathematician Bhāskara, who is presumed to have lived about A. D. 1114 to 1178.—*K. S. Markley, Southern Regional Research Laboratory.*